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Sleep-Disordered Breathing in Down Syndrome

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OSA is associated with significant adverse outcomes with far-reaching health-care implications. OSA is much more common and severe in patients with Down syndrome (DS) than in the general population, yet there is a striking lack of literature in this area. In this review article, we have summarized the current state of knowledge and presented the available data on OSA in DS. The higher prevalence and severity of OSA in patients with DS may be related to unique upper airway anatomic features as well as increased risk for obesity, hypothyroidism, gastroesophageal reflux disease, and generalized hypotonia. Although many of the manifestations of OSA in patients with DS are similar to those seen in the general population, the relative morbidity is significantly higher. For individuals with DS who already face cognitive challenges, the added impact of OSA on cognitive function may hinder their ability to function independently and reach their full potential. Screening and evaluation for OSA should be done in children and adults with DS. Treatment of OSA in DS involves the use of CPAP, upper airway surgery, and dental appliances, along with weight-reduction strategies, nasal steroids, and oral leukotriene modifiers as adjunctive treatments. The treatment plan should be individualized for each patient with DS, taking into account age, comorbid conditions, and barriers to treatment adherence. Future research should aim to better characterize OSA, further evaluate neurocognitive outcomes, and evaluate the efficacy of treatments in patients with DS.

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ABBREVIATIONS: AD = Alzheimer disease; AHI = apnea-hypopnea index; AT = adenotonsillectomy; BPAP = bilevel positive airway pressure; CSA = central sleep apnea; DS = Down syndrome; EF = executive function; PAP = positive airway pressure; PSG = polysomnogram; SDB = sleep-disordered breathing

Sleep-disordered breathing (SDB) refers to a group of disorders characterized by abnormalities of respiration and/or ventilation during sleep. It encompasses central sleep apnea (CSA) syndromes, OSA disorders, sleep-related hypoventilation disorders, and sleep-related hypoxemia disorder.[1] OSA is the commonest of these disorders and has been associated with significant adverse impacts on health, such as stroke, coronary artery disease, hypertension, arrhythmias, and excessive daytime sleepiness resulting in an increased risk of motor vehicle accidents.[2-5] It is increasingly being recognized that OSA is associated with memory impairment and deterioration in other aspects of cognitive functioning.[6]

Down syndrome (DS), defined by an extra copy of chromosome 21, is the commonest genetic disorder, occurring in one out of

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691 births.[7] Individuals with DS are at an increased risk of heart defects, gastroesophageal reflux, celiac disease, hypothyroidism, hearing and vision problems, leukemia, and Alzheimer disease (AD), as well as intellectual disability of varying degrees.

The prevalence of OSA in children with DS is 30% to 50% and increases to > 90% in adults with DS, as compared with the 2% to 4% prevalence seen in the general population.[8-10] In addition, OSA is usually more severe in patients with DS, with significant hypoxemia as compared with individuals without DS.[10] Several manifestations of OSA, such as cognitive impairment and cardiovascular disease, are common in individuals with DS, which may obscure the diagnosis of OSA in patients with DS. Thus, clinicians should maintain a high index of suspicion for OSA in patients with DS.

Adults with DS also have a very high risk of developing AD.[11] The added insult of OSA in this highly vulnerable population may exacerbate cognitive difficulties and lead to a greater predisposition to neurodegeneration.

Patients with DS now lead longer and more productive lives. Early recognition and aggressive treatment of OSA in patients with DS can further help to improve quality of life. Despite the significant resources that have been allocated to the study of OSA in the general population, few studies have evaluated the impact of OSA on patients with DS, and available studies are limited by small sample size.

Although not a systematic review, the purpose of this article is to provide a comprehensive review of this topic with a focus on recent developments in the field. Keywords such as "Down syndrome sleep disordered breathing" and "obstructive sleep apnea," and specific topics such as "cognitive functioning," "Alzheimer disease," and "executive functioning," and databases including PubMed, CINAHL, PsycINFO, and MEDLINE were used in searches, which were limited to English language. In addition to computer searches, the ancestry approach was used. An important goal of this article is to identify published information specific to OSA in individuals with DS; however, given the limited amount of research on OSA in those with DS, evidence regarding OSA in the general population is discussed to make recommendations for further research. Salient studies specifically addressing OSA in patients with DS are listed in Table 1.[8,10,12-28]

OSA and DS

Patients with DS are predisposed to upper airway obstruction due to multiple factors (Fig 1). Midface and maxillary hypoplasia have been demonstrated radiologically, resulting in smaller bony dimensions of the airway.[12,29] Although absolute tongue size is normal, relative macroglossia results because of the smaller bony framework of the small maxilla and mandible. Donnelly et al[13] demonstrated on cine MRI that this relative macroglossia and hypotonia resulted in airway obstruction caused by glossoptosis and hypopharyngeal collapse (also referred to as pharyngomalacia) in nearly two-thirds of children with DS and persistent OSA after adenotonsillectomy (AT). A follow-up study revealed that lingual tonsillar hypertrophy is > 10 times more common in children with DS compared with other children with OSA, further contributing to obstruction at the oropharyngeal level.[30] Hypotonia may also cause obstruction at the supraglottic level, with laryngomalacia being demonstrated in nearly 50% of children with DS and upper airway obstructive symptoms.[14] Subglottic and tracheal stenosis are more common in patients with DS than other populations.[15,31]

The association between obesity and OSA in individuals with DS has been demonstrated in several studies.[10,16,17] In a Dutch sample, children with DS were almost twice as likely to be overweight and obese as compared with a control group (25% of boys and 32% of girls with DS were overweight, and 4% of boys and 5% of girls were obese).[32] Women and men with DS were more likely to be overweight, with women more likely to be obese when compared with matched control subjects.[33] It is postulated that fat deposits in the lateral wall of the pharynx reduce the caliber of the upper airway and increase airway collapsibility. Central obesity, defined as increased intraabdominal and subcutaneous fat as measured by waist circumference, has been associated with OSA.[34,35] Individuals with DS have a higher incidence of central adiposity; however, the actual prevalence relative to the typical population needs further study. In another study, the apnea-hypopnea index (AHI) was found to be highly correlated with the degree of obesity in adults with DS.[10] Obesity is a risk factor for OSA and is more prevalent in patients with DS; thus, it has been suggested that OSA severity in those with DS may be correlated with obesity.[10,36] Therefore, obesity as a risk factor for OSA should be discussed with all patients with DS.

Higher rates of gastroesophageal reflux disease are seen in patients with DS, which can lead to inflammation and obstruction of the upper airway, thus increasing risk of developing OSA.[37,38] An increased OSA prevalence of 25% to 35% has been reported in the general population in patients with hypothyroidism.[39,40] This association